Developing breakthrough therapies in NASH, systemic sclerosis and mucopolysaccharidosis (MPS)

Jefferies 2018 Healthcare Conference

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Inventiva: a clinical stage biopharma with a focus on fibrosis

Three late stage clinical programs

Two royalty bearing collaborations with AbbVie and Boehringer Ingelheim

Pre-clinical pipeline in oncology and fibrosis

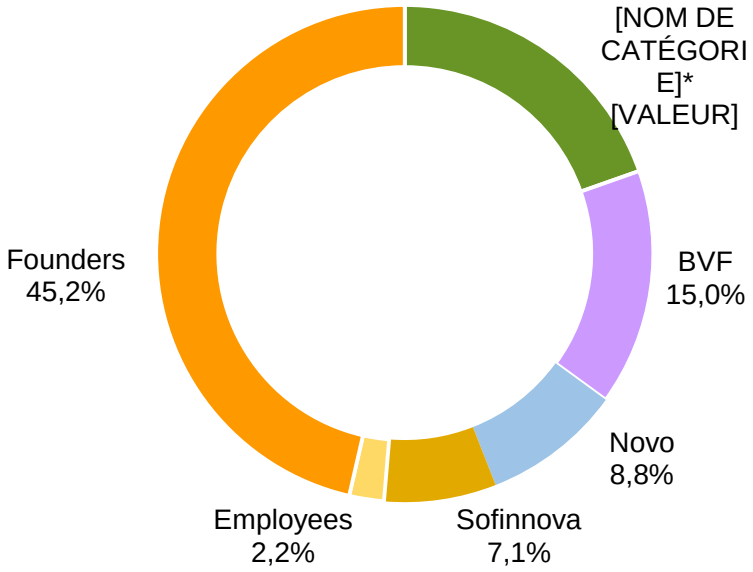
Listed on Euronext Paris

Strong cash position and shareholder base

Key financials

ISIN code	FR0013233012
Market	Euronext Paris
Shares outstanding	22,197,277
Market cap (27 May 2018)	€170m
Cash in 2017 (31 December 2017)	€59m (including €48.5m raised at the IPO) compared to €24.8m in 2016. Proforma cash position as of April 30, 2018 after the €32,5M capital increase amounts to €81.5 million
Revenues in 2017 (31 December 2017)	€6.5m (including €2.5m from Boehringer Ingelheim) compared to €9.4m in 2016
R&D expenditures in 2017 (31 December 2017)	€26.7m compared to €22.1m in 2016

Shareholder base



**Including Perceptive Advisors*

Analyst Coverage

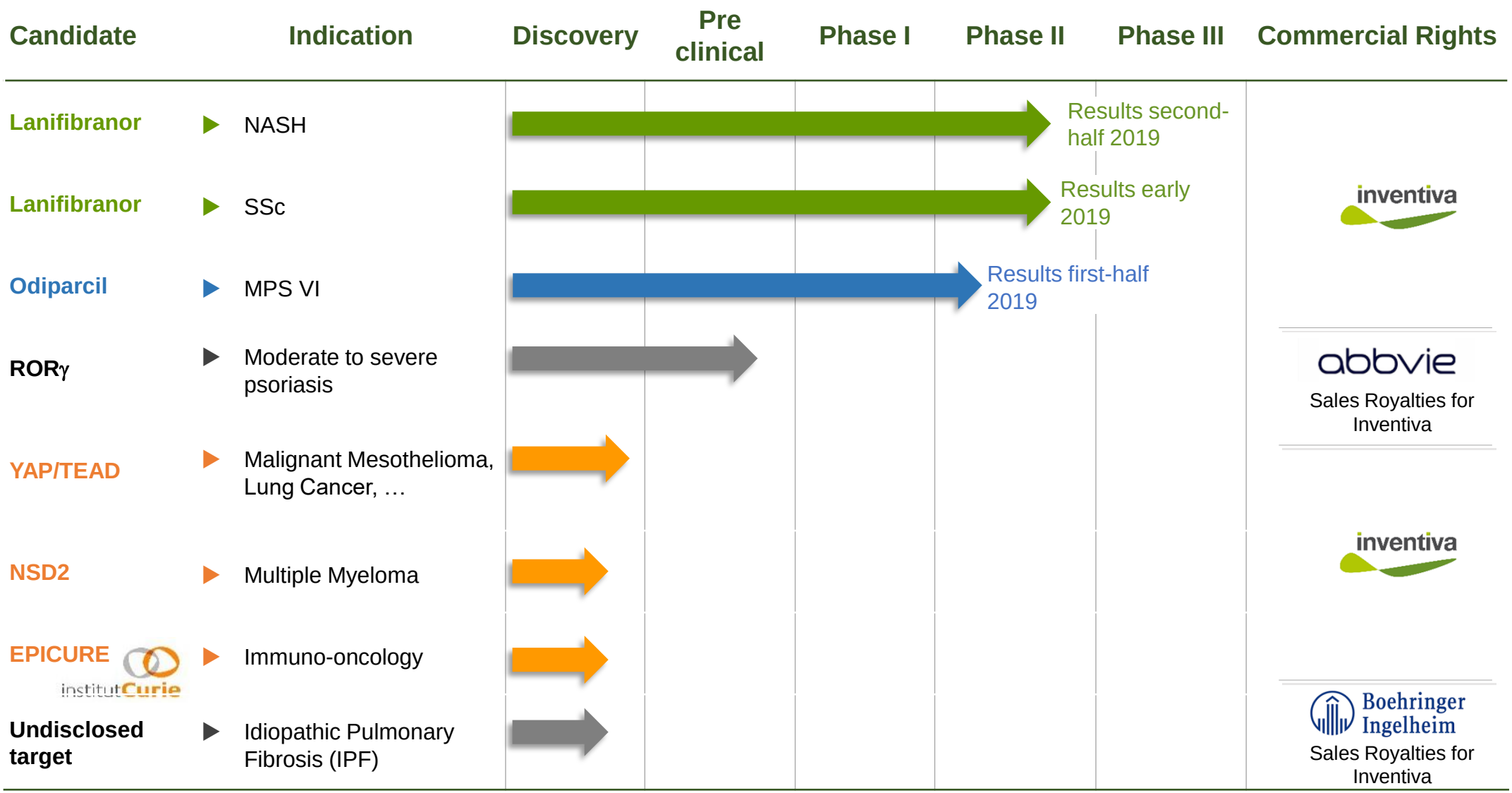
SOCIETE GENERALE Corporate & Investment Banking

GILBERT DUPONT

KBC

LIFESCI CAPITAL

Large pipeline reaching major inflection points



Lanifibranor NASH and SSc

A new generation pan-PPAR agonist for a safe and efficacious treatment of fibrotic conditions

Lanifibranor: a next generation panPPAR agonist for a safe and efficacious treatment of fibrotic conditions

Oral drug. 100 volunteers treated in phase I trials and 56 patients treated in phase IIa study

Phase IIb ongoing in NASH and systemic sclerosis (SSc)

NASH

- PPAR clinically validated targets with efficacy demonstrated on insulin resistance, steatohepatitis and fibrosis
- Phase IIa data demonstrating efficacy on key metabolic markers
- Preclinical data demonstrating beneficial effects on steatohepatitis and liver fibrosis, unique anti-fibrotic mechanism of action

SSc

- Anti-fibrotic activity demonstrated in skin, kidney, lung
- Beneficial effects on pulmonary arterial hypertension
- Orphans status granted in US and EU

Composition of matter patent granted in 59 countries: limit of exclusivity 2031

A good safety profile differing from previously developed PPARs

Different profile than other PPAR: moderate and balanced activity

Lanifibranor binds differently than rosiglitazone into the PPARγ ligand binding domain

Phase I and II studies underline the excellent tolerability of lanifibranor

- Good overall tolerance and no major safety findings
- No increases of creatinine, liver function test or LFTs, or creatine phosphokinase (CPK)
- No changes in blood pressure
- No signal of fluid overload or hemodilution
- No weight gain

Long term (6 and 12 Mo) non-clinical toxicological tox studies confirm the benign safety profile

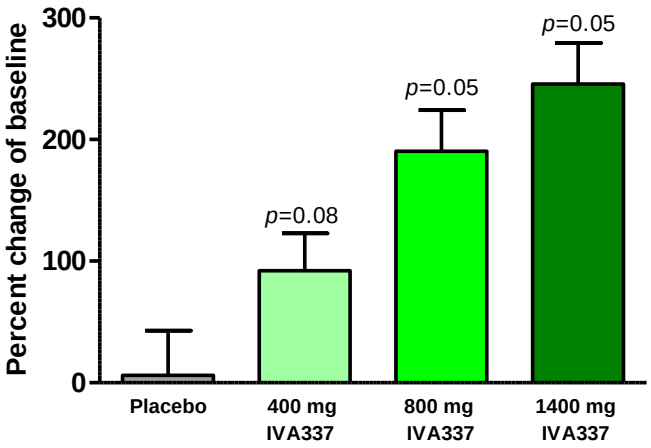
EMA allowed to run a 12 months study in man, even if the preclinical package only allowed to dose for 6 months

Phase IIa clinical studies demonstrated lanifibranor efficacy on key metabolic markers

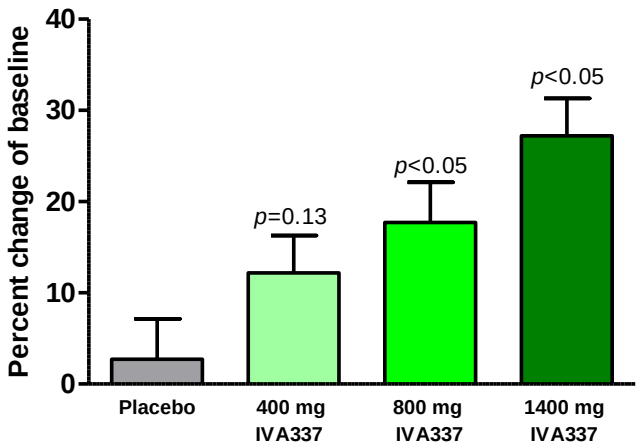
Lanifibranor (IVA337) strongly improves metabolic markers

- Insulin resistance (HOMA-IR, adiponectin)
- Dyslipidemia (increase in HDL-C, reduction of TG)

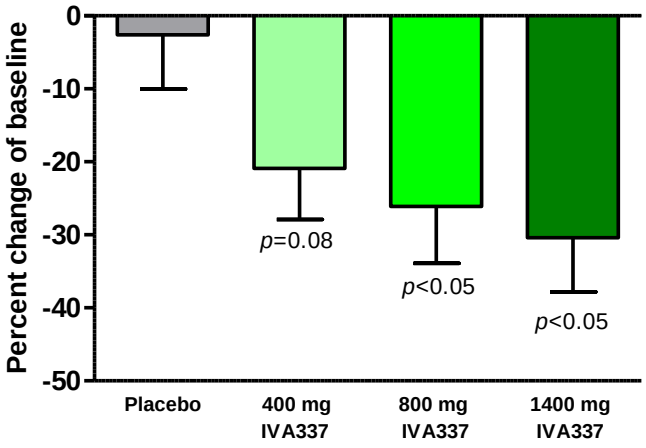
Adiponectin (PPARγ)



HDL Cholesterol (PPARα)



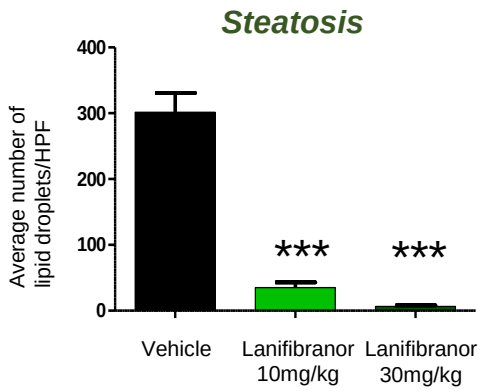
Triglycerides (PPARα/δ)

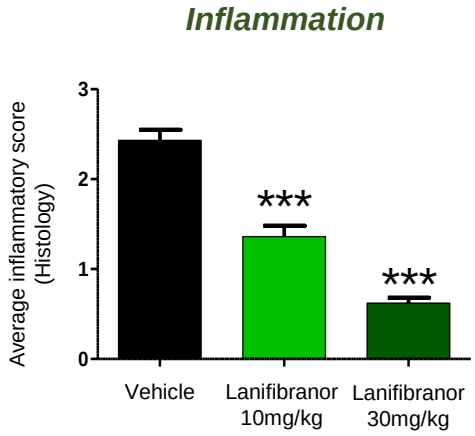


Source: Company data

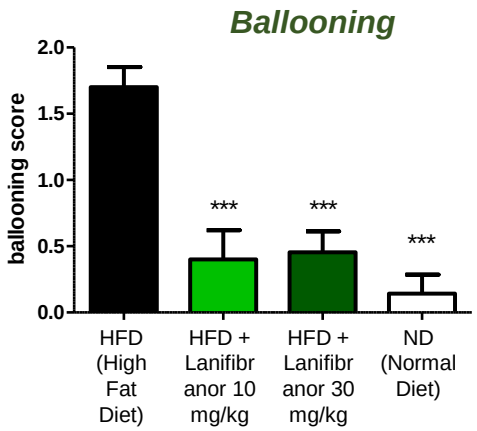
Lanifibranor strongly reduces steatosis, inflammation, ballooning and fibrosis in preclinical models

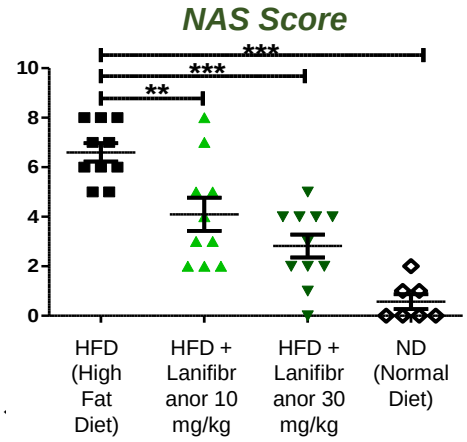
Lanifibranor inhibits steatosis and inflammation in the MCD model



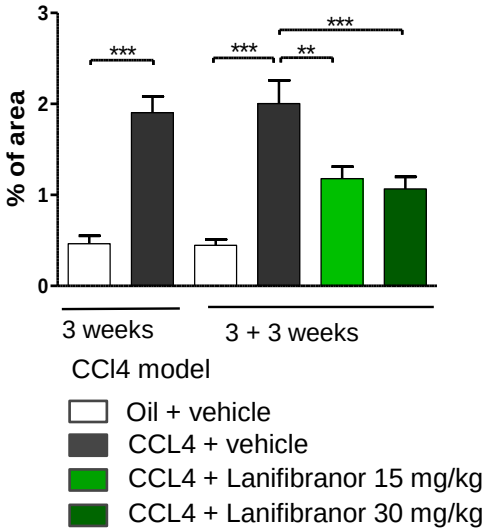


Lanifibranor strongly reduces ballooning and the NAS score in the foz/foz model





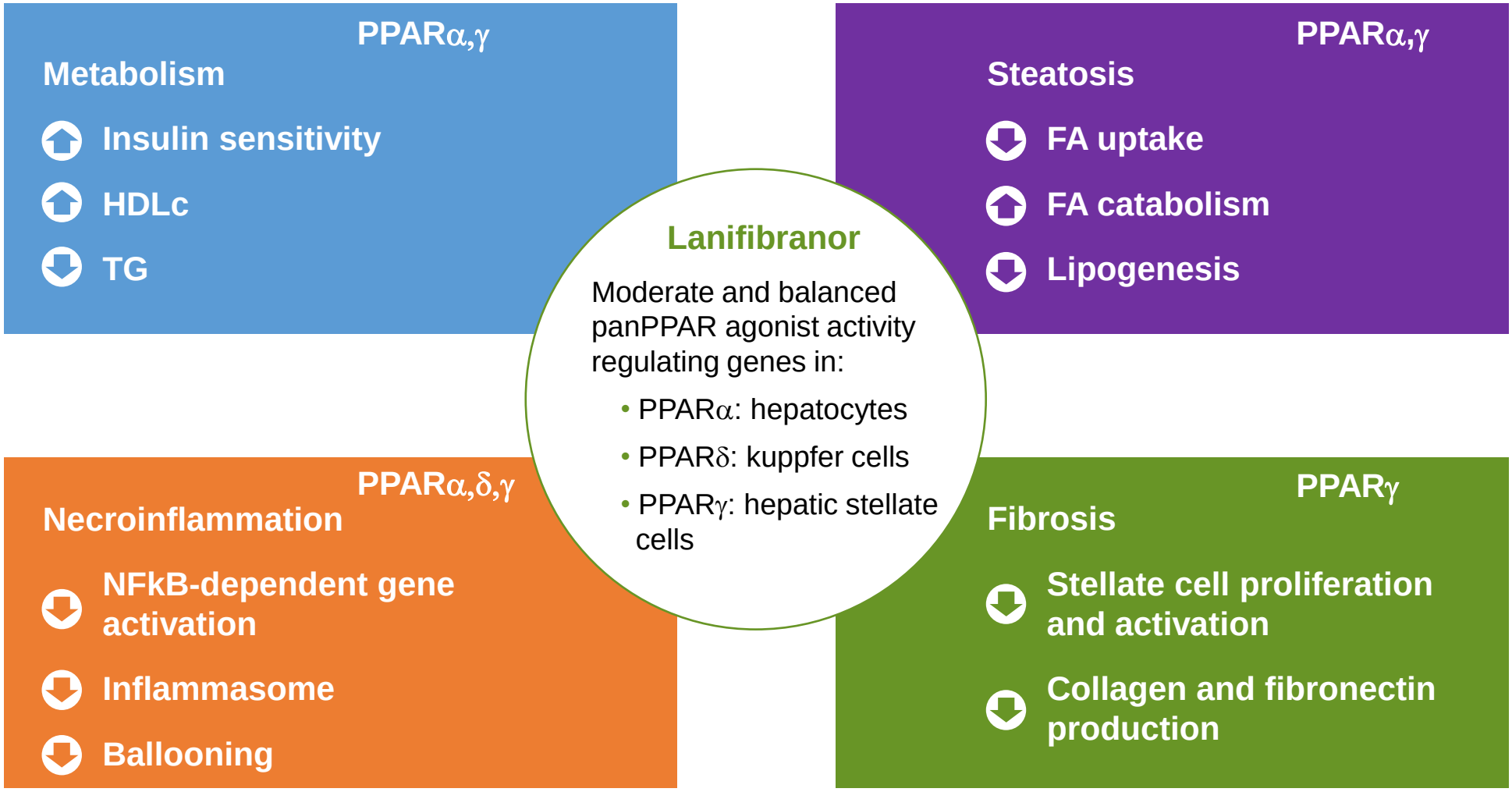
Lanifibranor reverses established liver fibrosis



Lanifibranor (IVA337) positively impacts all NASH-relevant liver lesions

Source: Company data; The new-generation Pan-Peroxisome Proliferator-Activated Receptor Agonist IVA337 Protects the Liver From Metabolic Disorders and Fibrosis; Hepatology Communications, June 2017

Lanifibranor: a mechanism of action addressing all the key features of NASH



NATIVE Phase IIb in NASH

Trial design

Principal investigator

- Pr Francque (Pr Francque (Universitair Ziekenhuis, Antwerpen, Belgium)

Status

- Trial enrolling
- Results expected second half 2019

Randomisation

- 1/1/1, stratification on T2DM patients
- Study powered with 75 patients per group

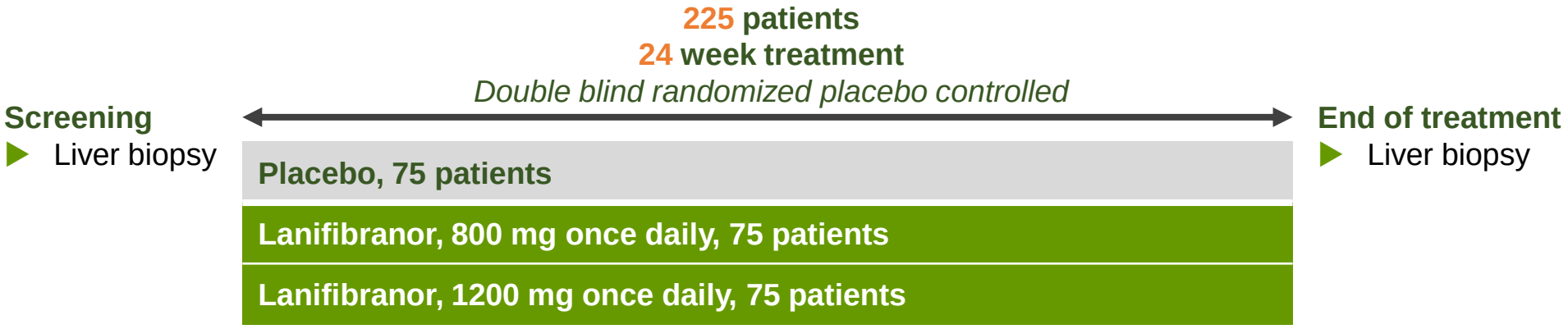
Inclusion criteria

- Liver biopsy
- Moderate to severe patients with a inflammation and ballooning score of 3 or 4
- Steatosis score ≥ 1 and fibrosis score < 4 (no cirrhosis)

Primary endpoint

- Decrease from baseline ≥ 2 points of the inflammation and ballooning score without worsening of fibrosis
- Central reading for pre- (before randomization) and post treatment biopsy

Clinicaltrials.gov identifier: NCT03008070



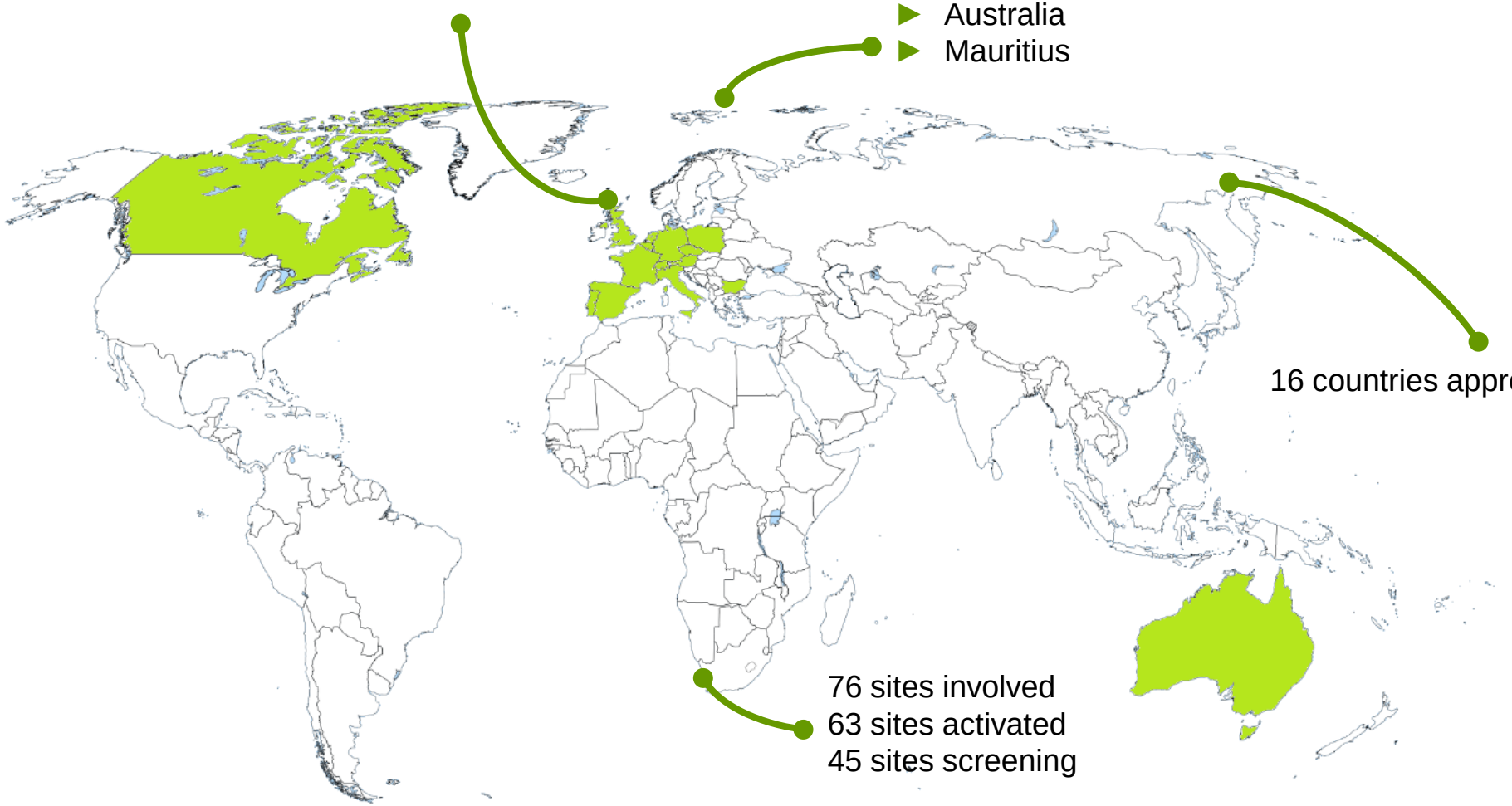
More information on: http://www.native-trial.com/

NATIVE: Phase IIb in NASH

NATIVE
NASH TRIAL TO VALIDATE IVA337 EFFICACY

16 countries worldwide
- 13 in EU
- Canada
- Australia
- Mauritius

Principal investigator: Pr Sven Francque, Belgium



16 countries approved

76 sites involved
63 sites activated
45 sites screening

Results expected second-half 2019

US investigator initiated Phase II trial in T2DM patients with NAFLD(1)

Trial design

Principal investigator

- Pr. Kenneth Cusi (University of Florida)

Design

- 24-week treatment period
- Two arms (placebo, lanifibranor 800 mg/day)
- Randomized (1:1), double-blind, placebo-controlled
- There is in addition a non-obese subject control group for the metabolic and imaging procedures

Sample size

- N= 64 calculated assuming a 35% relative reduction of IHGT(2)

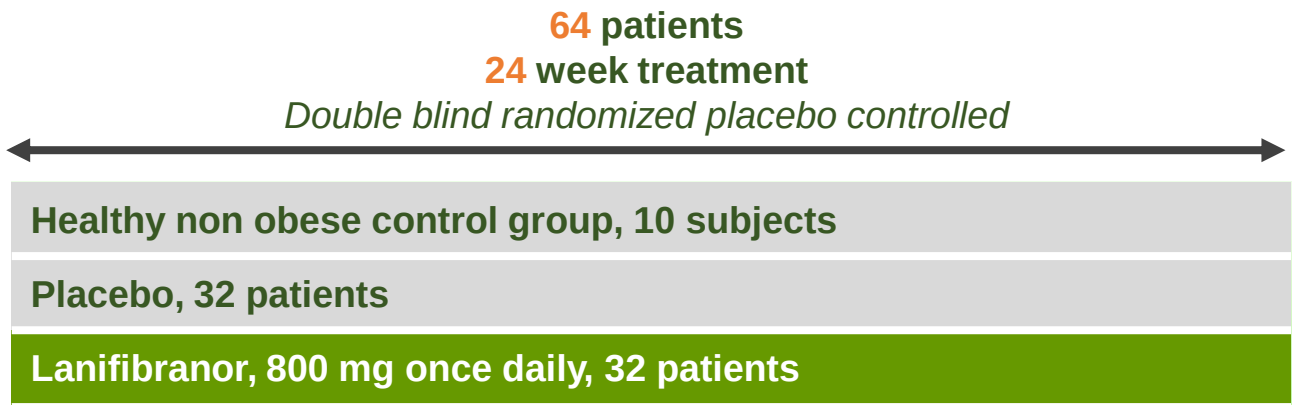
Primary endpoint

- Change from baseline to week 24 in IHTG

Key secondary endpoints

- Proportion of responders (IHTG, NAFLD resolution)
- Change in hepatic fibrosis (MRE(3), biomarkers)
- Change in metabolic outcomes (insulin sensitivity, DNL(4), glycemic control, lipids)
- Safety

Clinicaltrials.gov identifier: NCT03459079



(1) NAFLD: Nonalcoholic fatty liver disease (2) Intrahepatic triglycerides (3) Magnetic resonance elastography (4) De-novo lipogenesis

Systemic sclerosis overview

A severe disease: 50% of patients will die within 10 years from the first diagnosis(1)

No approved treatment

More than 170,000 patients diagnosed and a market potential > €1.8bn (2)

Clear regulatory pathway with the MRSS (Modified Rodnan Skin Score) accepted as approval endpoint (FDA and EMA)

Potential for conditional approval

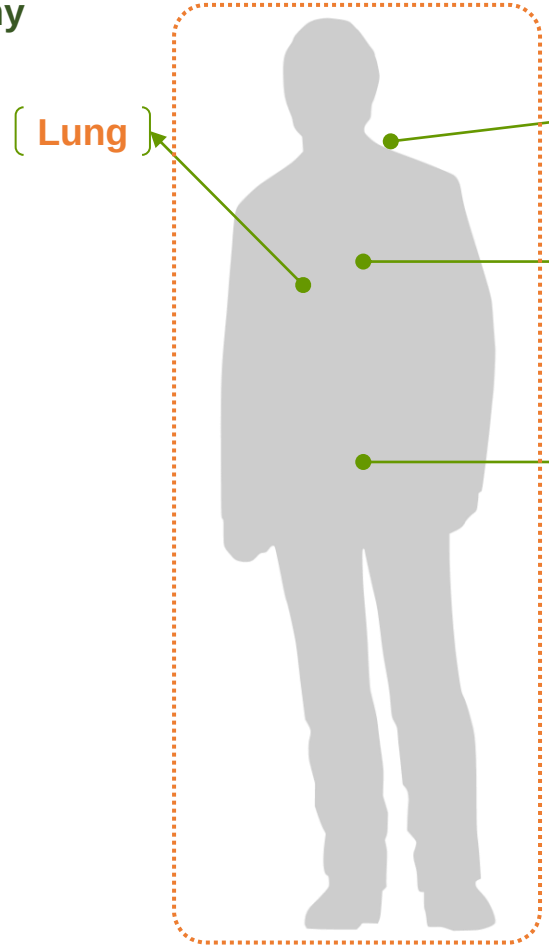
Source: (1) Eular SSc Trials and Research Group, EUSTAR, SSc Research Foundation, Canadian SSc research group ; (2) Venture Valuation.

Lanifibranor addresses all the relevant clinical features of systemic sclerosis

Lanifibranor reduces vasculopathy and inflammatory driven lung fibrosis

Lanifibranor restores lung functional capacity

Lanifibranor inhibits pulmonary arteries remodeling with positive impact on pulmonary artery pressure



Lanifibranor reduces established skin fibrosis

Lanifibranor reduces right ventricular systolic pressure and right ventricular hypertrophy

Lanifibranor reduces kidney fibrosis

FASST Phase IIb in SSc

Trial design

Principal investigator

- Principal investigators: Pr Allanore (Hôpital Cochin, Paris) and Pr Denton (University College of London)
- Other: Pr Matucci (Florence University, Italy), Pr Distler (University of Erlangen, Germany), Pr Distler (Universitaet Zurich, Switzerland)
- US scientific advisors: Pr John Varga (Northwestern University), Pr Dinesh Khanna (Michigan University)

Status

- Last patient recruited in October 2017
- Results expected early 2019

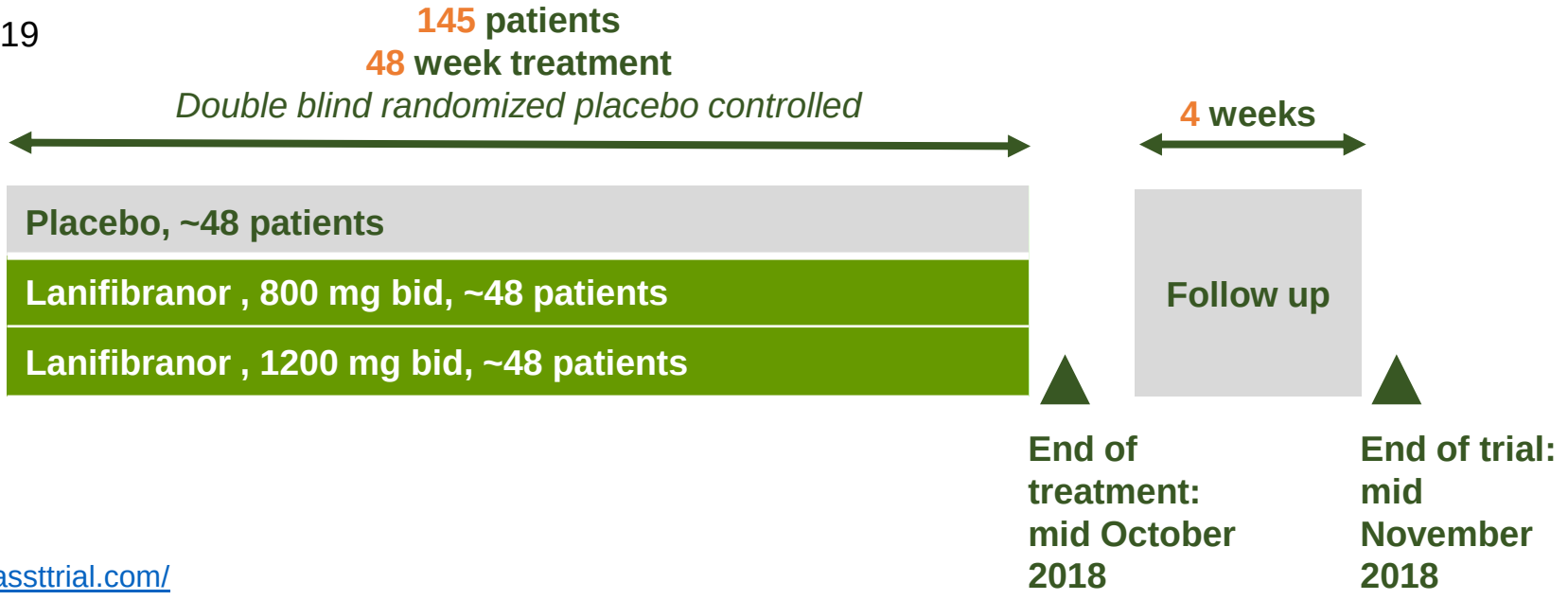
Inclusion criteria

- MRSS (Modified Rodnan Skin Score) between 10 and 25
- SSc diagnosed from less than 3 years

Primary endpoint

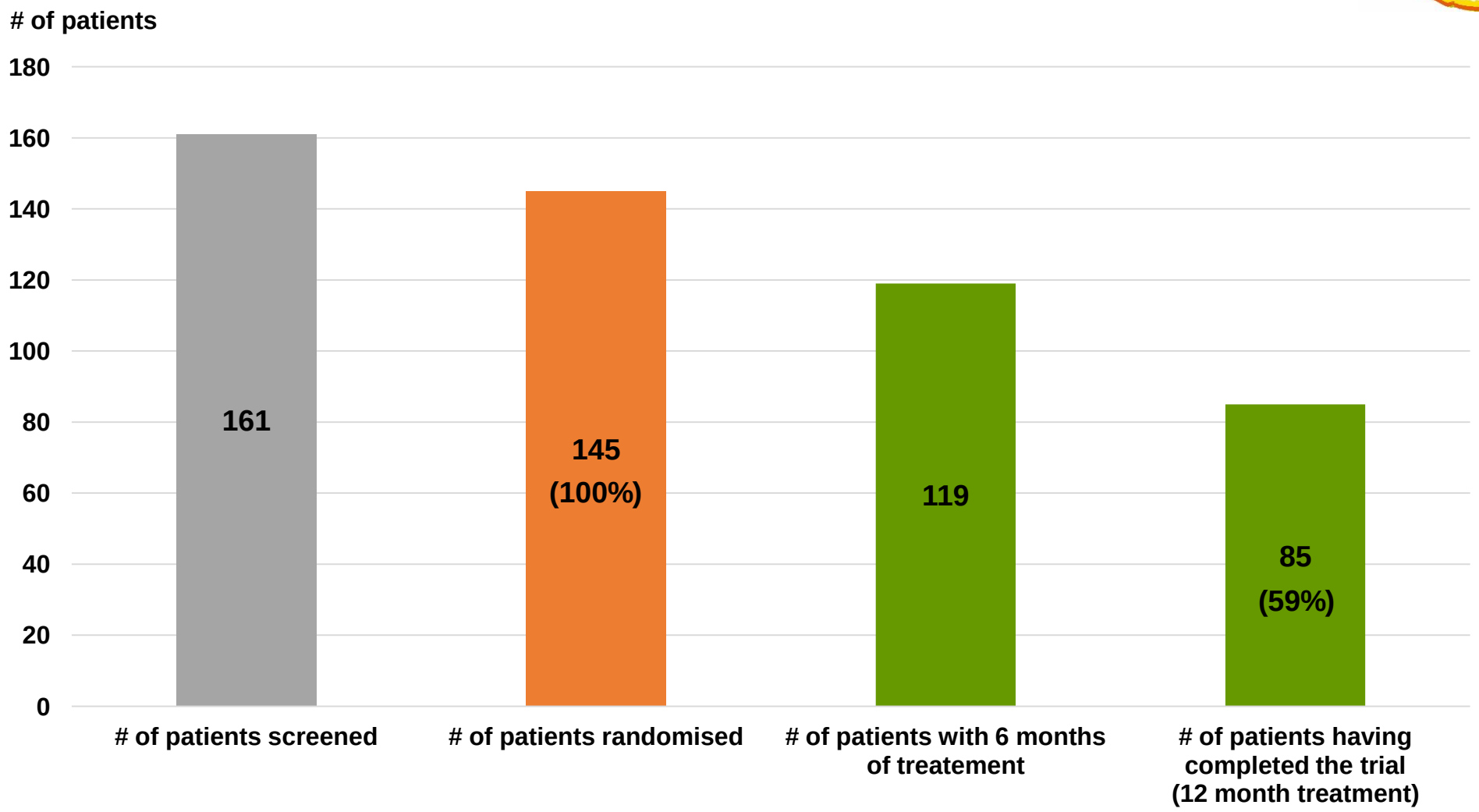
- Mean change of the MRSS from baseline to 48 weeks

Clinicaltrials.gov identifier: NCT02503644



More information on: http://www.fassttrial.com/

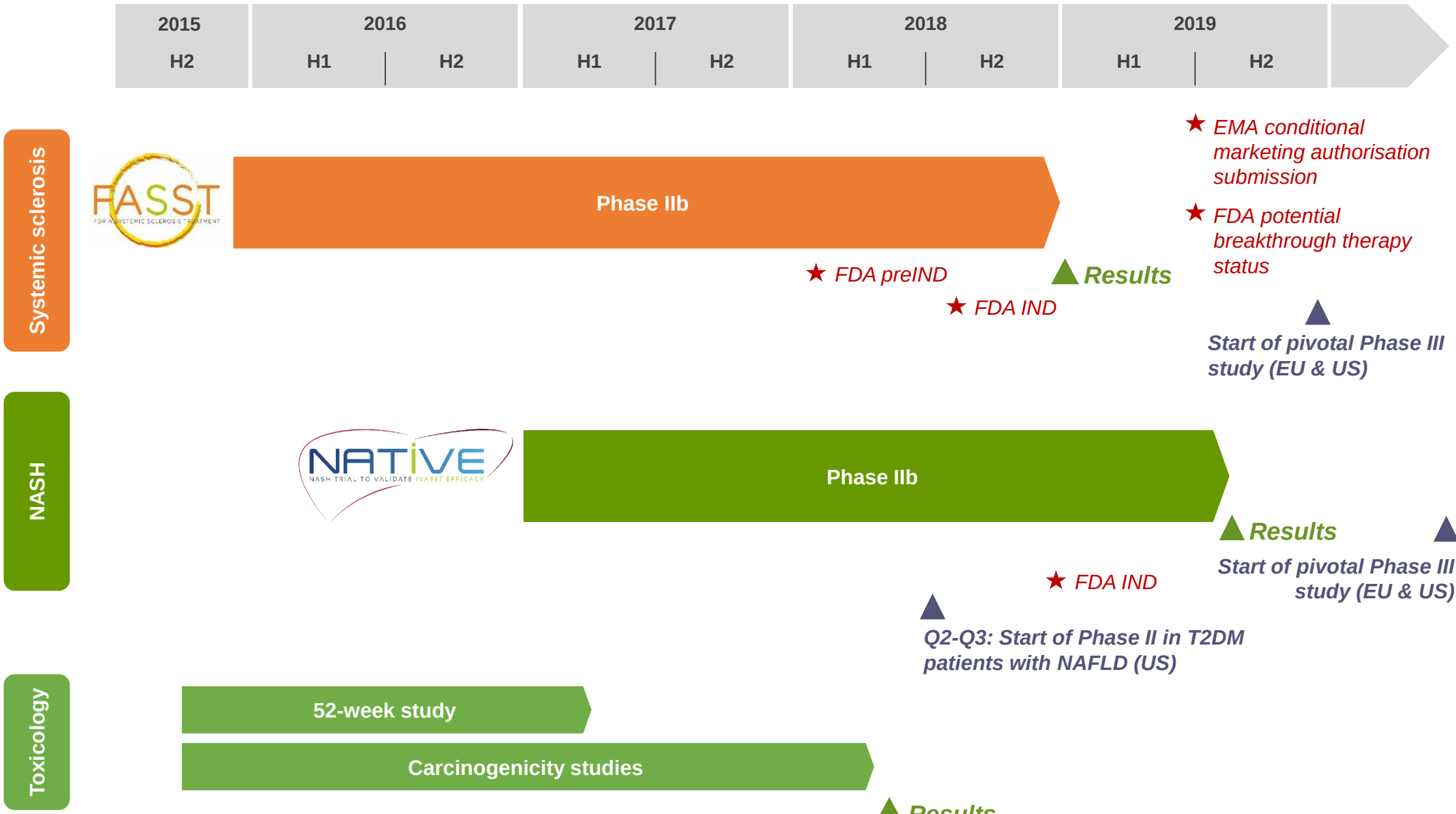
FASST: 100% of patients randomized and close to 60% of patients have already completed the trial(1)



Two positive DSMBs in January and April 2018 recommended to continue the study unchanged
Results expected early 2019

(1) Situation at May 28th 2018

Lanifibranor: a phase III ready program in both SSc and NASH by 2019



Start of FASST and NATIVE trials corresponds to first patient screened

Odiparcil

The first oral therapy to treat five forms of mucopolysaccharidosis (MPS): MPS I, II, IV, VI and VII

Odiparcil, the first oral therapy for several forms of MPS

- Oral drug with large phase I and phase II clinical package
- Novel mechanism of action allowing to reduce intra-cellular GAG content
- Efficacious in tissues and organs not treated by enzyme replacement therapies
- Potential to replace ERT in MPS VI patients
- Patent granted in the US and the EU with limit of exclusivity in 2039
- Orphan status granted in Europe and the US

By producing soluble chondroitin and dermatan sulfates, odiparcil can address several types of MPS

Type (Incidence)[1]	Name	Severity	Dermatan Accumulation	Chondroitin Accumulation	Heparan Accumulation	Keratan Accumulation	Other
MPS I-H (1/100 000)	Hurler syndrome	Most severe form	☑		☑		
MPS I-S (1/100 000)	Scheie syndrome	Mildest	☑				
MPS-IH/S (1/100 000)	Hurler-Scheie syndrome	More severe than MPS I-S, but less severe than MPS I-H	☑		In some cases		
MPS II Types A & B 1/100 000 to 1/170 000	Hunter syndrome Only MPS inherited as an X-linked trait	Type A more severe than B	☑		☑		
MPS III Types A to D 1/70 000	Sanfilippo syndrome	Severe			☑		
MPS IV Type A 1/200 000 to 300 000[2]	Morquio syndrome	Quite severe 95% of Morquio patients		☑		☑	
MPS IV Type B 1/200 000 to 300 000[2]	Morquio syndrome	Quite severe Type A more severe than B				☑	
MPS VI 1/250 000 to 600 000	Maroteaux-Lamy syndrome	Mild to severe	☑	☑			
MPS VII (1/250 000)	Sly syndrome	Mild to severe	☑	☑	☑		
MPS IX (rare)	Natowicz syndrome	Severe					Hyaluronic acid

MPS VI selected as first indication to demonstrate odiparcil efficacy

Source: raredisease.org ; (1) MPS society ; (2) for both type A and B

Odiparcil decreases GAG content *in vivo* and improves mobility in a MPS VI model

Wild-type and MPS VI mice
Treatment starts when animals are one month old

6 months

± Odiparcil*
Given in food

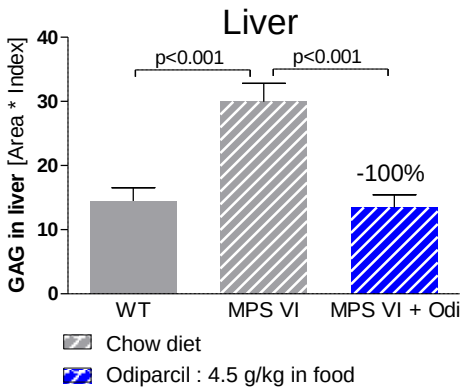
- Sulfated GAGs in organs/tissues and urine
- Mobility test
- Corneal structure/clouding

** The doses administered provides exposure levels similar to the one to be used in clinic*

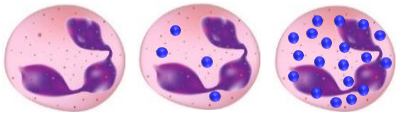
In vivo in MPS VI affected mice

- Odiparcil decreases GAG accumulation in various tissues and intracellular GAG accumulation in lymphocytes
- Odiparcil restores mobility
- Odiparcil decreases GAG accumulation in cornea, restores corneal structure and decreases GAG accumulation in cartilage

Odiparcil decreases GAG accumulation in tissues

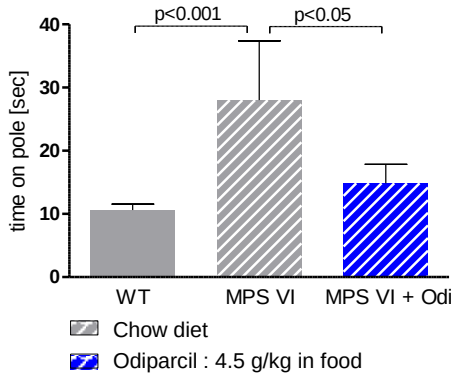


Odiparcil decreases intra-cellular GAG



GAG Granules:	0	1-10	>10
WT	40.4	45.8	9.4
MPS VI	15.1	32.6	51.3
MPS VI + Odi	19.7	47.4	21.5

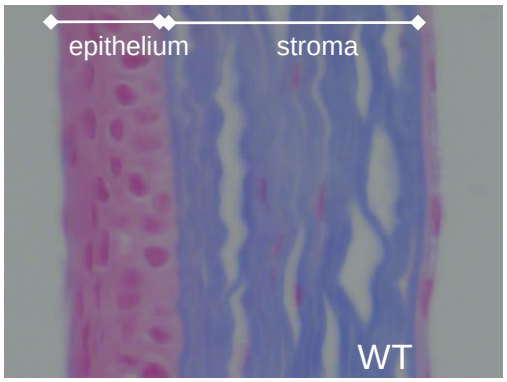
Odiparcil improves animal mobility

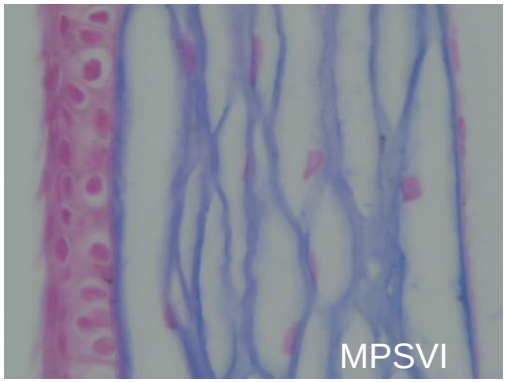


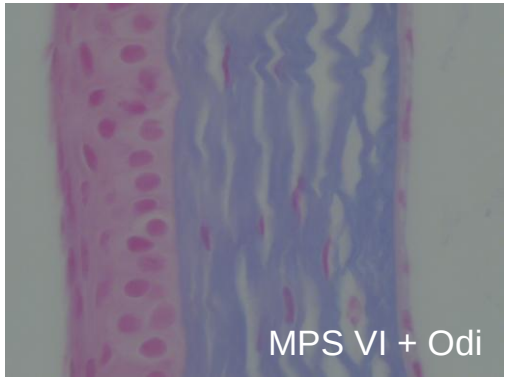
Odiparcil by decreasing GAG accumulation in tissues and cells should reduce GAG storage in MPS VI patients and improve their disease state

Source: Company data

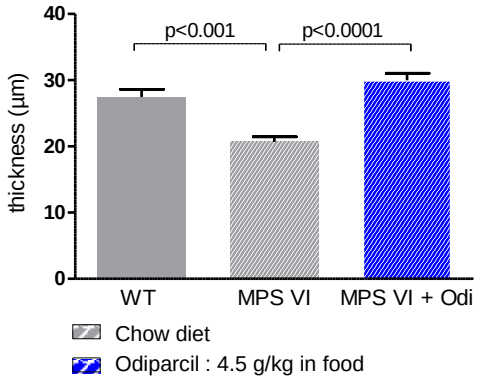
Odiparcil decreases corneal GAG accumulation and restores corneal structure



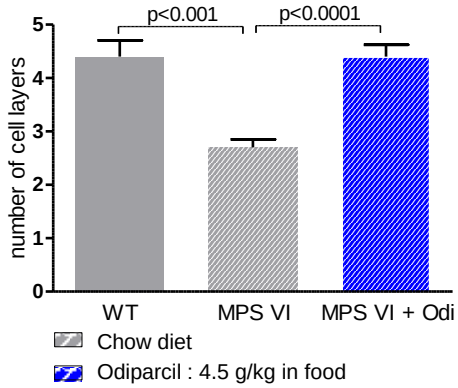




Odiparcil restores corneal epithelium thickness



Odiparcil restores corneal epithelium cell layers



Odiparcil decreases GAG storage in corneal stroma

Blinded corneal stroma vacuolation scoring

WT	0.0
MPS VI	2.9
MPS VI + Odi	0.5

scale (0-3)

0. no detectable vacuolation, no GAG accumulation
1. some large vacuolation with some distended cells
2. extensive area of large vacuolation with GAG accumulation
3. extensive area of large vacuolation with GAG accumulation and separate collagen fibers

Odiparcil by decreasing GAG storage and restoring corneal structure should restore corneal function and improve ocular impairment

Source: Company data

Odiparcil has the potential to positively differentiate versus current enzyme replacement therapies

	Odiparcil	Aldurazyme, Elaprase, Naglazyme, Vimizim, Mepsevii	HSCT (Hematopoietic stem cell transplantation)
Effect on mobility	✓	✓	✓
Eye, cartilage, bones, heart valves, spinal cord compression	✓	✗	✗
Safety	✓	✓	✗
Dose regimen	✓	✗	✗

Source: Company evaluation

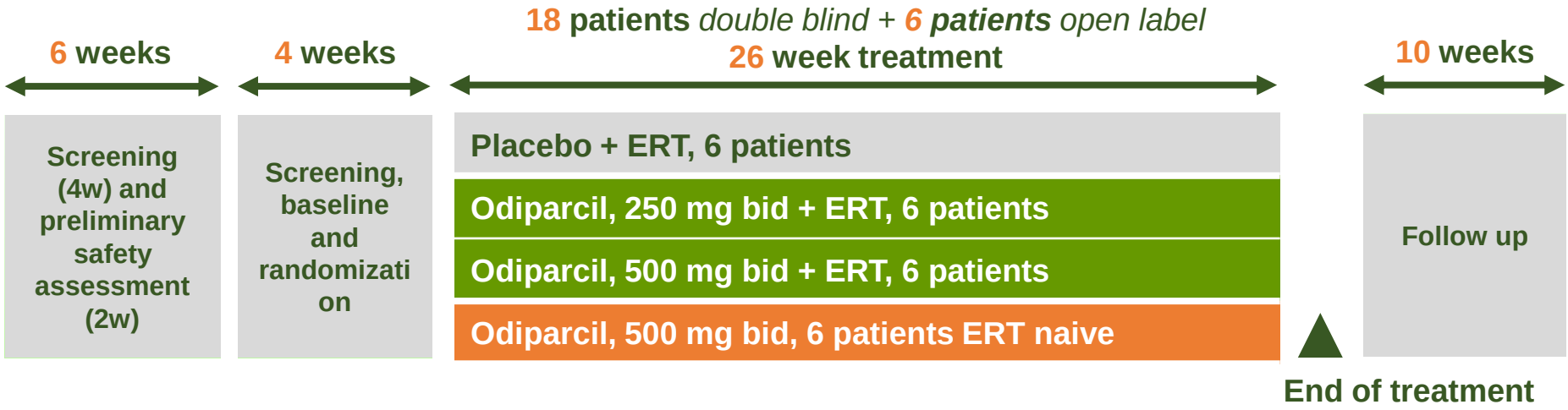
Odiparcil iMProveS phase IIa study in MPS VI patients

iMProveS
IMPROVE MPS TREATMENT

Trial design

- **Inclusion criteria:** MPS VI patients (≥ 16 year-old)
- **Status:** First patient recruited December 2017.

Clinicaltrials.gov identifier: NCT03370653



Endpoints

Safety

- Clinical and biological assessments (standard tests)

Pharmacokinetics

- Odiparcil plasma levels

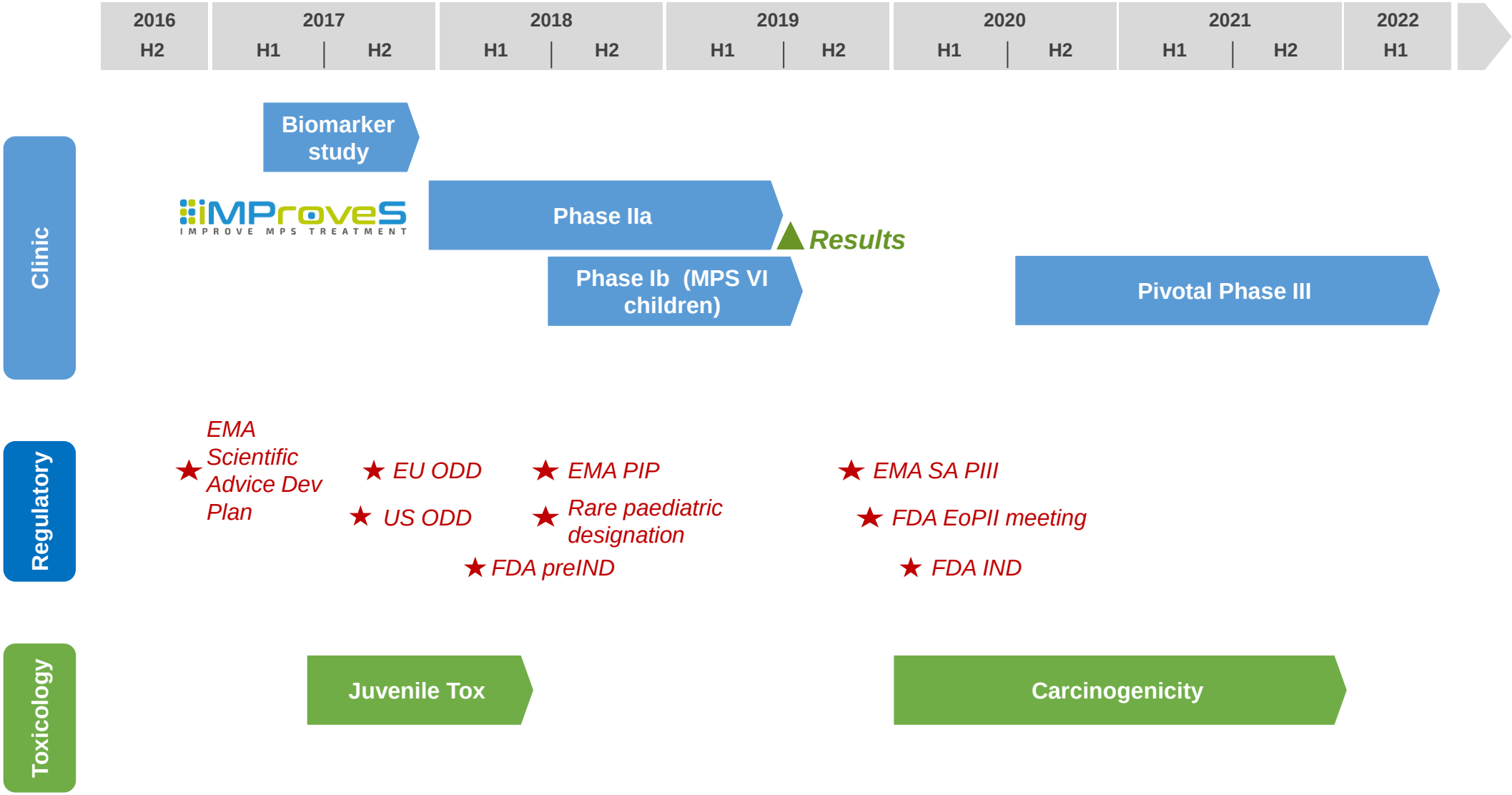
Efficacy

- Leukocyte, skin and urinary GAG content
- Activity and mobility tests (6 minutes walk test, upper limb function, shoulder mobility range)
- Cardiac, vascular and respiratory functions
- Eye impairment, hearing capacity, pain assessment, quality of life questionnaires

Results expected first semester 2019

More information on: http://www.improves-mpsvi-trial.com/

Odiparcil overall development plan in MPS VI



Start of iMProves trial corresponds to corresponds to first patient screened

Two collaborations with leading pharma companies

Two successful collaborations in place with AbbVie and Boehringer Ingelheim

RORγ collaboration

- RORγ program addresses large markets currently dominated by biologics
- RORγ could prove to be superior to biologics
- Inventiva and AbbVie identified clinical and preclinical compounds
- Inventiva eligible to multiple milestones payments and sales royalties on a product with block-buster potential

ABBV-157 expected to enter phase I in 2018

Collaboration in fibrosis

- Multi-year R&D collaboration and licensing partnership
- Joint team until pre-CC stage. BI to take full responsibility of clinical development and commercialization
- Following the validation of this new target supporting its therapeutic potential in fibrotic conditions, Boehringer Ingelheim exercised the option to jointly develop this target triggering a milestone payment of 2,5 M€
- Inventiva eligible to up to 170 M€ in milestones plus royalties

LO milestone expected in 2019

Near-term catalysts

Recent achievements and upcoming milestones

	2017	2018	2019
Lanifibranor	☑ 12 month monkey study finalized ☑ Lanifibranor INN name from WHO ☑ Last patient phase IIb SSc	▶ Last patient phase IIb NASH ▶ 2 year carcinogenicity study results ▶ SSc IND ▶ NASH IND ▶ Start US phase II in NAFLD	▶ **Results Phase IIb SSc** ▶ **Results Phase IIb NASH**
Odiparcil	☑ MPS patent granted in US ☑ US orphan status designation ☑ EU orphan status designation ☑ First patient Phase IIa in MPS VI	☑ MPS VI biomarker study results ▶ Rare pediatric disease designation MPS VI ▶ Start Phase Ib in children ▶ Juvenile tox results	▶ **Results Phase IIa MPS VI** ▶ **Results Phase Ib in children**
Collab.	☑ 2,5M€ milestone from Boehringer Ingelheim (option exercise) ☑ ABBV-157 preclinical nomination ☑ AbbVie RORγ collaboration renewal	▶ Start Phase I with ABBV-157	
Discovery	☑ Yap-Tead: in vivo activity obtained ☑ Epicure: target validated	▶ Yap-Tead: Vivo POC ▶ Epicure: HTL	▶ **Yap-Tead: start of Phase I/II enabling preclinical development**
Finance	☑ IPO on Euronext	☑ Capital increase	